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DEVELOPMENT AND CHARACTERIZATION OF ORAL COMBINATION VACCINE AGAINST HEPATITIS B & INFLUENZA

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Intro: Vaccination has not only become vital but a lot of revolutionary changes are being observable in the field of vaccine delivery. Vaccine antigens administered by the oral route are often degraded during gastrointestinal transit.

Methods: Bile salt stabilized vesicles i.e. bilosomes are found to be effective in preventing antigen degradation and enhance mucosal penetration. The aim of the present work was to prepare a combination vaccine system against hepatitis- B (HBsAg) and influenza(r-H1N1Ags). Bilosomes containing HBsAg and r-H1N1Ags were prepared by a lipid cast film method.

Findings: Antigen loaded bilosomes were characterized in-vitro for their shape, size, percent antigen entrapment and stability. Fluorescence microscopy was carried out to confirm the uptake of bilosomes. The in-vivo study comprised of estimation of IgG response in serum and sIgA in various body secretions using specific ELISA.

Discussion: Bilosomes formed were multilamellar and were stable in gastric and intestinal fluids. Fluorescence microscopy suggested that bilosomes were taken up by gut-associated lymphoid tissues. In-vivo data demonstrates that bilosomes produced both systemic as well as mucosal antibody responses upon oral administration at higher dose levels as compared to intramuscular immunization but fail to produce any synergistic effect.

Conclusion: Thus, HBsAg potentiates the production anti-r-H1N1 antibody. Also measurable sIgA in mucosal secretions were observed. Thus, bilosomes are a promising carrier for oral combination vaccines. This approach could be adapted for human use because mucosal surfaces are initial sites of infection and it therefore seems logical to attempt to develop vaccination strategies that evoke appropriate localized responses to counteract early events of pathogenesis.

https://doi.org/10.1016/j.ijid.2023.04.343

PHASE 3 STUDY OF SAFETY AND IMMUNOGENICITY OF GBP510 VACCINE ADJUVANTED WITH AS03 IN ADULTS

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Intro: GBP510 contains the self-assembling recombinant nanoparticle displaying SARS-CoV-2 Spike protein receptor binding domain and is adjuvanted with AS03. We report interim Phase 3 study (NCT05007951) results up to 4 weeks post-dose 2 (Data-cut: March-18-2022), where immunogenicity to the D614G ancestral strain and safety of 25μg GBP510/AS03 candidate was compared to ChAdOx1-S (Vaxzevria).

Methods: This Phase 3 randomized, active-controlled, observer-blind, parallel- group study in adults was conducted in 6 countries. Cohort1: 1,895 subjects (naïve to COVID-19 vaccination and infection) randomized at 2:1 ratio (GBP510/AS03:ChAdOx1-S) to assess immunogenicity and safety; Cohort 2: 2,141 subjects at 5:1 ratio, regardless of their serostatus at screening for safety assessment. Subjects were vaccinated twice at a 4-week interval with 0.5 mL of the test vaccine (GBP510/AS03) or active control (ChAdOx1-S) in deltoid muscle. The primary objective was to demonstrate the superiority of geometric mean titer (GMT) and non-inferiority in seroconversion rate (SCR: ≥4-fold rise from baseline) of neutralizing antibodies over ChAdOx1-S by live-virus neutralization assay (FRNT).

Findings: At 2 weeks post-dose 2, GMT ratio of the two groups (Test vaccine/Active control) was 2.93 [95% CI: 2.63, 3.27], satisfying the hypothesis of superiority (95% CI lower limit> 1). The SCR difference (Test vaccine – Active control) was 10.76% [95% CI: 7.68, 14.32], satisfying the hypothesis of non- inferiority (95% CI lower limit> -5%). Good cell-mediated immune responses for Th1 cytokines were also observed with the test vaccine (FluoroSpot). The AE incidence rate for the test vaccine was higher than the active control for solicited local AEs (56.69% vs 49.20%), and comparable for solicited systemic AEs (51.21% vs 53.51%) and unsolicited AEs (13.34% vs 14.66%) after any vaccination.

Conclusion: Higher immune responses were observed with GBP510/AS03 compared to ChAdOx1-S against D614G strain after 2 weeks post-dose 2. GBP510/AS03 showed a clinically acceptable safety profile; no safety concerns were identified during the study period.

https://doi.org/10.1016/j.ijid.2023.04.344

TEN-YEAR FOLLOW-UP OF MSSA TREATMENT PRESCRIPTION BEHAVIOR AND POST-PRESCRIPTION AMS INTERVENTION IMPACT

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Intro: Methicillin susceptibility prevails within clinically relevant Staphylococcus aureus strains. This study aimed to describe proportions of Methicillin- Susceptible S. aureus (MSSA), prescription behavior for its treatment, and impact of a post-prescription antimicrobial stewardship (AMS) strategy within two private tertiary care Mexican hospitals over 10 years.

Methods: Patients older than 14 years with an S. aureus culture-proven infection between 2011 to 2020 were included. Disease was classified as monomicrobial or polymicrobial; strains were classified as MSSA if Cefoxitin susceptible. Spectrum Score was calculated according to the participants' antibiotic regimen at: admission, 72 hours after culture results, and end-of- therapy. During the last two years analyzed, post-prescription review with feedback to prescribers as an AMS strategy. MSSA rates were compared within both time periods.

Findings: We identified 1322 clinically relevant S. aureus strains isolated from 2011 to 2020. A total of 817 specimens were MSSA (61.8%), while only 505 demonstrated methicillin resistance(38.2%). During the antimicrobial stewardship period, MSSA proportion increased by 21.6% compared to the pre- intervention period(78.9% vs 57.3%). In patients with monomicrobial MSSA infections, mean decrease Spectrum Score was lower at end of therapy in comparison to that calculated 72 hours after culture results(1.3 vs 0.2 points). The latter didn't seem to differ when contrasting the Spectrum score between the period before(0.3 points) and after(0.2 points) the AMS intervention. The three most commonly